

Mohamed

661696

=> fil med,hcap,biosis,embase,wpids;s (mas or meiosis activat? substance? or
dimethyl(5a)cholesta?(10a)triene(5a)ol or
dimethyl(3a)cholest?(10a)trien?(3a)ol(w)hemisuccin? or cholest?(5a)dien?(3a)ol or
cholest?(5a)dien?(5a)ol(a)hemisuccin? or cholest?(5a)diol
'MED' IS AN AMBIGUOUS FILE OR CLUSTER NAME
MEDICINE - Medicine and Medical Science Cluster
MEDICONF - Medical Conferences and Events worldwide
MEDLINE - MEDlars onLINE File from 1960 - present
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=> fil medl,hcap,biosis,embase,wpids;s mas or meiosis activat? substance? or
dimethyl(5a)cholesta?(10a)triene(5a)ol or
dimethyl(3a)cholest?(10a)trien?(3a)ol(w)hemisuccin? or cholest?(5a)dien?(3a)ol or
cholest?(5a)dien?(5a)ol(a)hemisuccin? or cholest?(5a)diol
COST IN U.S. DOLLARS

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ENTRY	SESSION
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L1	2996 FILE MEDLINE
L2	11897 FILE HCAPLUS
L3	3079 FILE BIOSIS
L4	2447 FILE EMBASE
L5	883 FILE WPIDS

TOTAL FOR ALL FILES

L6 21302 MAS OR MEIOSIS ACTIVAT? SUBSTANCE? OR DIMETHYL(5A) CHOLESTA?(10A
) TRIENE(5A) OL OR DIMETHYL(3A) CHOLEST?(10A) TRIEN?(3A) OL(W)
HEMISUCCIN? OR CHOLEST?(5A) DIEN?(3A) OL OR CHOLEST?(5A) DIEN?(5
A) OL(A) HEMISUCCIN? OR CHOLEST?(5A) DIOL

=> s hydroxy(4a)diemthyl(5a)cholest?(5a)dien?(5a)oic acid(5a)methionine amide

L7	0 FILE MEDLINE
L8	0 FILE HCAPLUS
L9	0 FILE BIOSIS
L10	0 FILE EMBASE
L11	0 FILE WPIDS

TOTAL FOR ALL FILES

Searched by: Mary Hale 308-4258 CM-1 1E01

L12 0 HYDROXY(4A) DIEMTHYL(5A) CHOLEST?(5A) DIEN?(5A) OIC ACID(5A)
METHIONINE AMIDE

=> s (ff mas or l6) and (?glycid? or phosph!!!glycid? or phospherglycid or
phosperglycid or amino acid or protein or peptide)

L13 485 FILE MEDLINE
L14 846 FILE HCAPLUS
L15 497 FILE BIOSIS
L16 371 FILE EMBASE
L17 68 FILE WPIDS

TOTAL FOR ALL FILES

L18 2267 (FF MAS OR L6) AND (?GLYCID? OR PHOSPH!!!GLYCID? OR PHOSPHERGLYC
ID OR PHOSPERGLYCID OR AMINO ACID OR PROTEIN OR PEPTIDE)

=> s l18 and (water or aqueous)

L19 33 FILE MEDLINE
L20 84 FILE HCAPLUS
L21 32 FILE BIOSIS
L22 27 FILE EMBASE
L23 15 FILE WPIDS

TOTAL FOR ALL FILES

L24 191 L18 AND (WATER OR AQUEOUS)

=> s (mas or meiosis activat? substance?) and
(dimethyl(5a)cholesta?(10a)triene(5a)ol or
dimethyl(3a)cholest?(10a)trien?(3a)ol(w)hemisuccin? or cholest?(5a)dien?(3a)ol or
cholest?(5a)dien?(5a)ol(a)hemisuccin? or cholest?(5a)diol)

L25 6 FILE MEDLINE
L26 9 FILE HCAPLUS
L27 7 FILE BIOSIS
L28 3 FILE EMBASE
L29 8 FILE WPIDS

TOTAL FOR ALL FILES

L30 33 (MAS OR MEIOSIS ACTIVAT? SUBSTANCE?) AND (DIMETHYL(5A) CHOLESTA?
(10A) TRIENE(5A) OL OR DIMETHYL(3A) CHOLEST?(10A) TRIEN?(3A)
OL(W) HEMISUCCIN? OR CHOLEST?(5A) DIEN?(3A) OL OR CHOLEST?(5A)
DIEN?(5A) OL(A) HEMISUCCIN? OR CHOLEST?(5A) DIOL)

=> dup rem l30

PROCESSING COMPLETED FOR L30

L31 19 DUP REM L30 (14 DUPLICATES REMOVED)

=> d cbib abs 1-19

L31 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2002 ACS

2002:615351 Process and container with low oxygen content and containing a
stable **MAS (meiosis activation
substances)** composition for increasing the fertility of oocytes
and use in IVF or IVM. Mueller, Lars Klingberg; Andersen, Tina Meinertz
(Novo Nordisk A/S, Den.). PCT Int. Appl. WO 2002062287 A1 20020815, 22
pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR,
BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB,
GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ,
VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF,
BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU,
MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.
APPLICATION: WO 2002-DK35 20020117. PRIORITY: DK 2001-189 20010206; DK

Searched by: Mary Hale 308-4258 CM-1 1E01

2001-382 20010308.

- AB A solid, stable compn. contg. a **meiosis activating substance** can be prep'd. by adding a protein or a phosphoglyceride in the presence of an atm. having a low content of oxygen, for example in vacuo. A closed container having a low content of oxygen and further contg. **MAS** is claimed. More specifically, a closed container having a low content of oxygen and further contg. a solid compn. with high aq. soly. comprising **MAS** and an additive is claimed. Also claimed is a process for prepg. a closed container having a low content of oxygen and further contg. a solid compn. comprising **MAS** and an additive.

L31 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2002 ACS

2002:486117 Document No. 137:42095 Process to increase concentration of meiosis-activating sterols (**MAS**) in cholesterol synthesis using potent inhibitors of .DELTA.24-redn. and/or 4.alpha.-demethylation. Lindenthal, Bernhard (Schering Aktiengesellschaft, Germany). Eur. Pat. Appl. EP 1216701 A1 20020626, 31 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR. (English). CODEN: EPXXDW. APPLICATION: EP 2000-250456 20001222.

- AB The invention relates to a process of increasing the concn. of meiosis-activating sterols (**MAS**) in cholesterol synthesis using potent inhibitors of .DELTA.24-redn. and/or 4.alpha.-demethylation. Pharmaceutical compns. comprising the potent inhibitors are also claimed. Since the **MAS** are responsible for the control of fertility the inhibitors can be used to treat infertility or as contraceptives. The inhibitors can also be used in the microbiol. prodn. of **MAS**. Progesterone, pregnenolone, 17.alpha.-hydroxypregnenolone, 17.alpha.-hydroxyprogesterone, 4-androsten-3,17-dione, testosterone, medroxyprogesterone, verapamil, tamoxifen, ursodeoxycholic acid, chenodeoxycholic acid, deoxycholic acid, lithocholic acid, cortisone, cortisol, 11-desoxycortisol, 17.beta.-estradiol, aldosterone, dehydroepiandrosterone, norethynodrel, 11-deoxycorticosterone, corticosterone, 6-amino-2-n-pentylthiobenzothiazole or mixts. of them are claimed as inhibitors.

L31 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2002 ACS

DUPLICATE 1

2002:54471 Document No. 136:278180 Production of Meiosis-Activating Sterols from Metabolically Engineered Yeast. Xu, Ran; Wilson, William K.; Matsuda, Seiichi P. T. (Department of Chemistry and Department of Biochemistry and Cell Biology, Rice University, Houston, TX, 77005, USA). Journal of the American Chemical Society, 124(6), 918-919. (English) 2002. CODEN: JACSAT. ISSN: 0002-7863. Publisher: American Chemical Society.

- AB Meiosis-activating sterols (**MAS**), a class of potent regulators of reproductive processes, are difficult to obtain by chem. synthesis or isolation from natural sources. We demonstrate the development of metabolically engineered strains of *Saccharomyces cerevisiae* that accumulate **MAS** as the predominant sterol product. Homologous recombination was used to construct an *erg24.DELTA. erg25.DELTA. hem1.DELTA. mutant RXY4.3*, which lacked sterol .DELTA.14 reductase, C-4 oxidase, and .delta.-aminolevulinate synthase. The *HEM1* deletion allowed sterol import and rendered *RXY4.3* viable under aerobic conditions. This mutant accumulated 4,4-dimethyl-5.alpha.-cholesta-8,14,24-trien-3.beta.-ol (**FF-MAS**), and a similar *erg25.DELTA. hem1.DELTA. mutant* produced 4,4-dimethyl-5.alpha.-cholesta-8,24-dien-3.beta.-ol (**T-MAS**). Based on consistent yields of approx. 5 .mu.g of **FF-MAS** per mL of culture, fermn. of genetically modified yeast compares favorably with other approaches to produce **MAS**.

L31 ANSWER 4 OF 19 MEDLINE

DUPLICATE 2

2002248295 Document Number: 21984476. PubMed ID: 11988327. Role of meiosis activating sterols, **MAS**, in induced oocyte maturation. Byskov Anne Grete; Andersen Claus Yding; Leonardsen Lise. (Laboratory of Reproductive Biology, Section 5712, Juliane Marie Center for Children, Women and Reproduction, Rigshospitalet, University Hospital of Copenhagen, Blegdamsvej 9, DK-2100, Copenhagen, Denmark.) MOLECULAR AND CELLULAR ENDOCRINOLOGY, (2002 Feb 22) 187 (1-2) 189-96. Journal-code: 7500844. ISSN: 0303-7207. Pub. country: Ireland. Language: English.

AB Meiosis of follicle enclosed oocytes is maintained in the prophase of the first meiotic division and oocytes do not spontaneously resume meiosis during oocyte growth and follicle development. Arrest of the meiotic process is most likely secured by the presence of follicular purines, e.g. hypoxanthine, which maintain high levels of cAMP in the oocyte and which also in vitro prevent oocytes from resuming meiosis. Only in response to the mid-cycle surge of gonadotropins will oocytes of preovulatory follicles overcome the meiosis arresting effect of hypoxanthine and resume meiosis proceeding to the metaphase of the second meiotic division. Morphologically, resumption of meiosis is observed by the disappearance of the oocyte's nuclear membrane (germinal vesicle), a process called germinal vesicle breakdown (GVB). The molecular mechanism down-stream to receptor activation by which the mid-cycle surge of gonadotropins induces oocytes to resume meiosis is, however, only partly understood. The oocyte itself lacks gonadotropin receptors and its action is mediated through the attached cumulus cells. In vitro it has been shown that FSH induces synthesis of a signal in the cumulus cells, which overcomes the meiosis arresting effect of hypoxanthine. We have shown that a group of sterols, meiosis activating sterols (**MAS**), induces oocyte maturation in vitro even in oocytes depleted of cumulus cells. **MAS** were identified as intermediates in the cholesterol biosynthesis between lanosterol and cholesterol. The two best characterized members of the **MAS** family are FF-**MAS** purified from human follicular fluid (4,4-dimethyl-5alpha-cholest-8,14,24-triene-3beta-ol) and T-**MAS** purified from bull testicular tissue (4,4-dimethyl-5alpha-cholest-8,24-diene-3beta-ol). The synthesis, quantification, localization and tissue-accumulation of **MAS** are reviewed. Several publications have documented the pharmacological effect of **MAS** in different species, including oocytes from mouse, rat and human. Conflicting results obtained by the use of sterol synthesis inhibitors, which prevent **MAS**-accumulation, are also discussed. Whether FSH actually uses **MAS** as a signal transduction molecule for inducing oocyte maturation and the mechanism by which **MAS** induce resumption of meiosis is currently unknown, but data to support that **MAS** is part of the FSH induced signal transduction pathway are presented.

L31 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
2001:208095 Document No. 134:242674 Composition for in vitro IVF containing a meiosis-activating substance. Andersen, Tina Meinertz (Novo Nordisk A/s, Den.). PCT Int. Appl. WO 2001019354 A2 20010322, 11 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-DK500. 20000911. PRIORITY: DK 1999-1308 19990916.

AB A compn. useful in connection with in vitro fertilization (IVF) based on a solid meiosis-activating substance (**MAS**) or a deriv. thereof with low soly. is described. A **MAS** can be dissolved in an aq. medium using an additive, e.g., a

protein or a phosphoglyceride, to obtain a soln. contg. at least 0.001 .mu.g/mL and not more than 0.1 g/mL of **MAS**. For example, solns. were prepd. by mixing (a) 100 .mu.L of ethanolic 4,4-dimethyl-5.alpha.-cholesta-8,14,24-triene-3.beta.-ol (FF-**MAS**) contg. 5.22, 2.5, or 0.5 .mu.g/mL FF-**MAS** and (b) 250 .mu.L of 20% aq. human serum albumin (HSA) in the ratio of FF-**MAS** to HSA of 1:10,000, 1:6667, and 1:2000, resp., and tested on oocytes obtained from immature female mice. Percent of germinal vesicle breakdown (GVB) for the formulations prepd. were 78, 82, and 90%, resp.

L31 ANSWER 6 OF 19 WPIDS (C) 2002 THOMSON DERWENT

AN 2002-017402 [02] WPIDS

AB WO 200176360 A UPAB: 20020109

NOVELTY - A nuclear maturation inhibiting substance (1), and at least one gonadotropin (2) and/or at least one growth factor (3) is used for the preparation of a cell culture medium for in vitro maturation of oocytes, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the in vitro maturation of oocytes involving:

- (a) culturing at least one GV oocyte in the culture medium;
- (b) washing the GV oocyte of (a) to remove (1), and
- (c) culturing the washed oocyte of (b) in the culture medium and/or meiosis activating sterol (**MAS**) to cause nuclear maturation.

The culture medium comprises (1), (2), and/or (3).

ACTIVITY - None given.

MECHANISM OF ACTION - **MAS** inhibitor or antagonist; nuclear maturation inhibitor.

Immature female mice (B6D2-F1 strain C57B1/2J) were kept under light and temperature. Ovarian stimulation was performed when the mice weighed 10-16 g and consisted of an intra-peritoneal injection of Gonadoplex containing 7.5 U/mouse. The animals were killed by cervical dislocation 44-48 hour later. The media used for the culture of oocytes consisted of alpha -minimum essential medium with Earles balanced salt solution, dibutyryl-cyclic adenosine-mono-phosphate (200 micro M), bovine serum albumin (3 mg/ml), pyruvate (0.23 mM), glutamine (2 mM), penicillin (100 IU/ml) and streptomycin (100 mg/ml) (i.e. control medium). The ovaries were recovered and the oocytes were isolated from the ovaries. The oocytes were washed 3 times with the control medium. Cumulus enclosed oocytes were cultured separately in 4-well dishes, 0.4 ml medium in each well containing control medium or medium supplemented with ketoconazole at 37 deg. C for 22-24 hours. The % of oocytes with germinal vesicle breakdown per total no of oocytes was calculated. To the control medium follicle stimulating hormone (FSH) (75 IU/L) was added. To the medium containing FSH (75 IU/L) increasing concentration of ketoconazole was added (i.e. 5, 10 and 20 micro M) and all media's were cultured with mouse oocytes. The results showed that the percent of GVBD achieved by FSH (75 IU/L) is higher than any of the other group. The % of GVBD between groups with ketoconazole and the control are all similar. The % of polar body formation is higher in the group receiving FSH alone compared to the control group and the group receiving ketoconazole in 10 and 20 micro M.

USE - For preparation of an oocyte (preferably GV oocyte) culture medium for in vitro maturation of the oocyte (claimed) of the mammal.

ADVANTAGE - The culture medium improves the viability and pregnancy potential of oocytes and pre-embryos obtained in connection with in vitro maturation, in vitro fertilization and pre-embryo transfer treatment. The culture medium stops or blocks selectively and reversibly, the nuclear maturation of oocytes and achieves a balanced and synchronized cytoplasmatic and nuclear maturation.
Dwg.0/1

L31 ANSWER 7 OF 19 WPIDS (C) 2002 THOMSON DERWENT

AN 2001-565401 [63] WPIDS

AB WO 200162260 A) UPAB: 20011031

NOVELTY - The use of 4,4-dimethyl-5a-cholesta-8,14,24-triene-3 beta -ol (FF-MAS) or its analogs for making a medication to increase the implantation rate of pre-implantational embryos is new.

ACTIVITY - Gynecological.

Fifteen mature female Wistar rats were used in a controlled study of 20 mg/kg intravenous FF-MAS and FF-MAS succinate given from 1 day proestrus, daily for 8 days. The animals were mated in the second day of the injections. The implantation rates at day 16 were control 10 plus or minus 4%, FF-MAS 15 plus or minus 3% and FF-MAS succinate 12 plus or minus 2%.

MECHANISM OF ACTION - None given.

USE - Useful for increasing the pregnancy rate and fertility in women with fertility problems. Also useful for increasing the implantation and pregnancy rate in animals important for breeding.

ADVANTAGE - The medication can help increase in-vivo pregnancy rates by up to 20% and avoid lengthy in-vitro fertilization procedures for women with fertility problems.

Dwg.0/0

L31 ANSWER 8 OF 19 WPIDS (C) 2002 THOMSON DERWENT

AN 2001-565400 [63] WPIDS

AB WO(200162258 A)UPAB: 20011031

NOVELTY - The use of 4,4-dimethyl-5a-cholesta-8,14,24-triene-3 beta -ol (FF-MAS) or its analogs to increase the implantation rate of pre-implantational embryos is new.

ACTIVITY - Gynecological.

Fifteen mature female Wistar rats were used in a controlled study of 20 mg/kg intravenous FF-MAS and FF-MAS succinate given from 1 day proestrus, daily for 8 days. The animals were mated in the second day of the injections. The implantation rates at day 16 were control 10 plus or minus 4%, FF-MAS 15 plus or minus 3% and FF-MAS succinate 12 plus or minus 2%.

MECHANISM OF ACTION - None given.

USE - Useful for increasing the pregnancy rate and fertility in women with fertility problems, and improving in-vitro fertilization success rates. Also useful for increasing the implantation and pregnancy rate in animals important for breeding.

ADVANTAGE - The medication can help increase in-vivo pregnancy rates by up to 20% and avoid lengthy in-vitro fertilization procedures for women with fertility problems as well as improve the in-vitro fertilization implantation rates by up to 50%.

Dwg.0/0

L31 ANSWER 9 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

2001:99780 Document No.: PREV200100099780. Meiosis-activating sterol and the maturation of isolated mouse oocytes. Downs, Stephen M. (1); Ruan, Benfang; Schroepfer, George J., Jr.. (1) Biology Department, Marquette University, 530 N 15 St., Milwaukee, WI, 53233: downss@marquette.edu USA. Biology of Reproduction, (January, 2001) Vol. 64, No. 1, pp. 80-89. print. ISSN: 0006-3363. Language: English. Summary Language: English.

AB This study was carried out to examine the effects of the meiosis-activating C29 sterol, 4,4-dimethyl-5alpha-cholesta-8,14,24-trien-3beta-ol (FF-MAS), on mouse oocyte maturation in vitro. Cumulus cell-enclosed oocytes (CEO) and denuded oocytes (DO) from hormonally primed, immature mice were cultured 17-18 h in minimum essential medium (MEM) containing 4 mM hypoxanthine plus increasing concentrations of FF-MAS. The sterol induced maturation in DO with an optimal concentration of 3 mug/ml but was without effect in CEO, even at concentrations as high as 10 mug/ml. Some stimulation of maturation in hypoxanthine-arrested CEO was observed when MEM was replaced by MEMalpha.

Interestingly, the sterol suppressed the maturation of hypoxanthine-arrested CEO in MEM upon removal of glucose from the medium. FF-MAS also failed to induce maturation in DO when meiotic arrest was maintained with dibutyryl cAMP (dbcAMP). The rate of maturation in FF-MAS-stimulated, hypoxanthine-arrested DO was slow, as more than 6 h of culture elapsed before significant meiotic induction was observed, and this response required the continued presence of the sterol. Although the oocyte took up radiolabeled lanosterol, such accumulation was restricted by the presence of cumulus cells. In addition, lanosterol failed to augment FSH-induced maturation and was even inhibitory at a high concentration. Moreover, the downstream metabolite, cholesterol, augmented the inhibitory action of dbcAMP on maturation in both CEO and DO. Two inhibitors of 14alpha-demethylase, ketoconazole, and 14alpha-ethyl-5alpha-cholest-7-ene-3beta,15alpha-diol that can suppress FF-MAS production from lanosterol failed to block consistently FSH-induced maturation. These results confirm the stimulatory action of FF-MAS on hypoxanthine-arrested DO but do not support a universal meiosis-inducing function for this sterol.

L31 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 4
 2000:628250 Document No. 133:188459 Meiosis activating sterol augments implantation rate. Andersen, Claus Yding; Byskov, Anne Grete (Den.). PCT Int. Appl. WO 2000052142 A2 20000908; 33 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DE, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-DK80 20000225. PRIORITY: DK 1999-273 19990226.

AB The present invention relates to the use of a new principle for improving the viability and pregnancy potential of oocytes and pre-embryos obtained in connection with in vitro fertilization and pre-embryo transfer treatment. More specifically, improvement by raising the content of Meiosis Activating Sterols (MAS) in the medium where the in vitro fertilization takes place. This is achieved by exposing and culturing one or more oocytes with spermatozoa in a culture medium comprising at least one meiosis activating sterol (MAS), a MAS analog, and/or an additive or additives capable of endogenous stimulation of the accumulation of at least one MAS. Preferred additives are FSH and EGF.

L31 ANSWER 11 OF 19 WPIDS (C) 2002 THOMSON DERWENT
 AN 2000-579147 [54] WPIDS
 AB WO 200050066 A UPAB: 20001027

NOVELTY - A human in vitro fertilization method, comprising treating a woman with a hypothalamic hormone and/or pituitary hormone, an antagonist or agonist of them, or an active derivative of them, within a consecutive 30 day period, and aspirating oocytes and actively maturing or synchronizing them in vitro in contact with a MAS compound which mediates oocyte meiosis, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a kit, in unit dosage form, for use in in vitro fertilization. The kit comprises separate dosage units for sequential daily administration of a hypothalamic hormone and/or pituitary hormone, an antagonist or agonist of them, or an active derivative of them, and one dosage unit of a MAS compound.

ACTIVITY - Enhancement of fertility. No biological data is given.

MECHANISM OF ACTION - None given.

USE - For the treatment of human infertility (claimed).

The process can improve maturation of human oocytes, improve the synchrony of nuclear, cytoplasmic and/or membranous oocyte maturation, improve the fertility of oocytes, improve the rate of implantation of oocytes, diminish the incidence of human preembryos with chromosome abnormalities, improve the cleavage rate of human preembryos and improve the quality of human preembryos.

Dwg.0/0

L31 ANSWER 12 OF 19 WPIDS (C) 2002 THOMSON DERWENT

AN 2000-579146 [54] WPIDS

AB WO 200050065 A UPAB: 20001027

NOVELTY - Human in vitro fertilization method comprising treating a woman for less than 7, preferably less than 4, days with a hypothalamic hormone and/or a pituitary hormone, or an agonist, antagonist or active derivative of them, and using in vitro oocyte maturation in which an egg or eggs are retrieved from the woman and are matured using a **MAS** compound which mediates oocyte meiosis, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a kit, in unit dosage form, for use in in vitro fertilization. The kit comprises 1-8 separate unit dosages. The kit comprises at least 1 but less than 7 (preferably less than 4) separate dosage units for sequential daily administration of a hypothalamic hormone and/or a pituitary hormone, or an agonist, antagonist or active derivative of them, and comprises one dosage unit of a **MAS** compound.

ACTIVITY - Enhancement of fertility. No biological data is given.

MECHANISM OF ACTION - None given.

USE - For the treatment of human infertility (claimed), and to improve maturation of human oocytes, improve the synchrony of nuclear, cytoplasmic and/or membranous oocyte maturation, improve the fertility of oocytes, improve the rate of implantation of oocytes, diminish the incidence of human preembryos with chromosome abnormalities, improve the cleavage rate of human preembryos and to improve the quality of human preembryos.

ADVANTAGE - The process reduces the side effects associated with prior art in vitro fertilization methods, in which GnRH is used for about 22 days and FSH is used for about 9 days before the eggs are retrieved. In the new process the period in which the female patient is treated with component A is reduced by 80-90 %, and the total period of treatment can be reduced by 50-60 %.

Dwg.0/0

L31 ANSWER 13 OF 19 MEDLINE

DUPLICATE 5

2000254109 Document Number: 20254109. PubMed ID: 10793639. Effect of inhibition of sterol delta 14-reductase on accumulation of meiosis-activating sterol and meiotic resumption in cumulus-enclosed mouse oocytes in vitro. Leonardsen L; Stromstedt M; Jacobsen D; Kristensen K S; Baltzen M; Andersen C Y; Byskov A G. (Laboratory of Reproductive Biology, Juliane Marie Center for Children, Women and Reproduction, Rigshospitalet, Blegdamsvej, Denmark.) JOURNAL OF REPRODUCTION AND FERTILITY, (2000 Jan) 118 (1) 171-9. Journal code: 0376367. ISSN: 0022-4251. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Two sterols of the cholesterol biosynthetic pathway induce resumption of meiosis in mouse oocytes in vitro. The sterols, termed meiosis-activating sterols (**MAS**), have been isolated from human follicular fluid (FF-**MAS**, 4,4-dimethyl-5 alpha-cholest-8,14,24-triene-3 beta-ol) and from bull testicular tissue (T-**MAS**, 4,4-dimethyl-5.alpha-cholest-8,24-diene-3 beta-ol). FF-**MAS** is the first intermediate in the cholesterol biosynthesis from lanosterol and is converted to T-**MAS** by sterol delta 14-reductase. An inhibitor of delta 7-reductase and delta 14 reductase, AY9944-A-7, causes cells with a constitutive cholesterol biosynthesis to accumulate FF-**MAS** and possibly other intermediates between lanosterol and

cholesterol. The aim of the present study was to evaluate whether AY9944-A-7 added to cultures of cumulus-oocyte complexes (COC) from mice resulted in accumulation of **MAS** and meiotic maturation. AY9944-A-7 stimulated dose dependently (5-25 μ mol l⁻¹) COC to resume meiosis when cultured for 22 h in alpha minimal essential medium (alpha-MEM) containing 4 mmol hypoxanthine l⁻¹, a natural inhibitor of meiotic maturation. In contrast, naked oocytes were not induced to resume meiosis by AY9944-A-7. When cumulus cells were separated from their oocytes and co-cultured, AY9944-A-7 did not affect resumption of meiosis, indicating that intact oocyte-cumulus cell connections are important for AY9944-A-7 to exert its effect on meiosis. Cultures of COC with 10 μ mol AY9944-A-7 l⁻¹ in the presence of [3H]mevalonic acid, a natural precursor for steroid synthesis, resulted in accumulation of labelled FF-**MAS**, which had an 11-fold greater amount of radioactivity incorporated per COC compared with the control culture without AY9944-A-7. In contrast, incorporation of radioactivity into the cholesterol fraction was reduced 30-fold in extracts from the same oocytes. The present findings demonstrate for the first time that COC can synthesize cholesterol from mevalonate and accumulate FF-**MAS** in the presence of AY9944-A-7. Furthermore, AY9944-A-7 stimulated meiotic maturation dose dependently, indicating that FF-**MAS**, and possibly other sterol intermediates of the cholesterol synthesis pathway, play a central role in stimulating mouse oocytes to resume meiosis. The results also indicate that oocytes may not synthesize steroids from mevalonate.

L31 ANSWER 14 OF 19 WPIDS (C) 2002 THOMSON DERWENT

AN 1999-620372 [53] WPIDS

CR 1999-509721 [43]

AB WO 9952930 A UPAB: 20020704

NOVELTY - 4,4-Dimethyl-5 alpha -cholesta-8,14,24-trien-3 beta -ol of the formula (1) is produced from a 3-oxopregn-4-ene-21-carboxylic acid derivative of formula (2) by a multi-stage process via new intermediates of formula (3)-(15).

DETAILED DESCRIPTION - Production of 4,4-dimethyl-5 alpha -cholesta-8,14,24-trien-3 beta -ol of formula (1) comprises:

- a) reacting a 3-oxopregn-4-ene-21-carboxylic acid derivative of formula (2) with a methylating agent in the presence of a base;
 - b) reducing the resulting 4,4-dimethyl-3-oxopregn-5-ene-21-carboxylic acid derivative of formula (3);
 - c) protecting the 4,4-dimethyl-3 beta -hydroxy-pregn-5-ene-21-carboxylic acid derivative of formula (4);
 - d) dehydrogenating the resulting 4,4-dimethyl-pregn-5-ene-21-carboxylic acid derivative of formula (5);
 - e) isomerising the 4,4-dimethyl-pregna-5,7-diene-21-carboxylic acid derivative of formula (6) obtained;
 - f) alkylating the resulting 4,4-dimethyl-pregna-8,14-diene-21-carboxylic acid derivative of formula (7);
 - g) reducing the 4,4-dimethyl-cholesta-8,14,24-triene-21-carboxylic acid derivative of formula (8) obtained;
 - h) sulfonating the resulting 4,4-dimethyl-cholesta-8,14,24-triene-21-ol derivative of formula (9); and
 - i) converting the sulfonated 4,4-dimethyl-3-cholesta-8,14,24-triene-21-ol derivative of formula (10) into compound (I) by reduction (when R² = H) or by reduction to the 4,4-dimethyl-3-cholesta-8,14,24-triene derivative of formula (11) and cleavage of the protecting group (when R² = protecting group).
- R¹ = H; 1-6C alkyl; phenyl; benzyl; or o-, m- or p-tolyl;
R² = aliphatic or aromatic carboxylic acid ester; acetal; or silyl;
R³ = SO₂R⁴;
R⁴ = 1-6C alkyl; phenyl; benzyl; o-, m- or p-tolyl; or 2,4,6-trimethylphenyl.

INDEPENDENT CLAIMS are also included for: (A) the preparation of

compound (1) by:

j) alkylating a 4,4-dimethyl-pregn-5,7-diene-21-carboxylic acid derivative (6);

k) reducing the resulting 4,4-dimethyl-pregn-5,7,24-triene-21-carboxylic acid derivative of formula (12);

l) sulphonating the 4,4-dimethyl-pregn-5,7,24-triene-21-ol derivative of formula (13) obtained;

m) reducing the resulting sulphonated 4,4-dimethyl-pregn-5,7,24-triene-21-ol derivative of formula (14) and

n) converting the resulting 4,4-dimethyl-pregn-5,7,24-triene derivative of formula (15) into compound (1) by isomerisation (when R2 = H) or isomerisation and cleavage of the protecting group in the resulting compound (11) (when R2 = protecting group); and

(B) new intermediates of formulae (3); (4); (5), (6) and (7) (R2 = H; aliphatic or aromatic carboxylic ester; or silyl); (8), (9), (10), (12), (13), (14) and (15) (R2 = H; aliphatic or aromatic carboxylic ester; acetal; or silyl); and (11).

ACTIVITY - None given.

MECHANISM OF ACTION - Meiosis regulator.

USE - Compound (I) (FF-MAS), known from Nature 1995, 374, 559, is useful as a fertility promoter. New intermediates (3)-(15) are also useful in chemical syntheses, e.g. for the preparation of FF-MAS analogues (see WO 9600235).

ADVANTAGE - The process requires fewer steps than the processes known from J. Am. Chem. Soc. 1989, 111, 278 and Bioorg. Med. Chem. Lett. 1997, 8, 233 and it does not require any expensive equipment.
Dwg.0/0

L31 ANSWER 15 OF 19 MEDLINE DUPLICATE 6
1999408759 Document Number: 99408759. PubMed ID: 10477894. Quantitation of meiosis activating sterols in human follicular fluid using HPLC and photodiode array detection. Baltzen M; Byskov A G. (Laboratory of Reproductive Biology, JMC, The Rigshospital, Blegdamsvej 9, DK-2300 Kobenhavn O, Denmark. mogens.lrb@notes.rh.dk). BIOMEDICAL CHROMATOGRAPHY, (1999 Oct) 13 (6) 382-8. Journal code: 8610241. ISSN: 0269-3879. Pub. Country: ENGLAND: United Kingdom. Language: English.
AB A chromatographic assay for 4,4-dimethyl-5alpha-cholesta-8,14, 24-triene-3beta-ol (FF-MAS), and its reduced species, 4, 4-dimethyl-5alpha-cholesta-8,24-triene-3beta-ol (T-MAS), has been established for analysis of human follicular fluid (huFF). The assay also quantifies lanosterol, free cholesterol and progesterone. It was established using a pool of more than 100 individual follicular fluids from women undergoing in vitro fertilization treatment. Both FF-MAS and T-MAS were found in huFF, and can be quantified with HPLC equipped with photodiode array (PDA) detection. The examination wavelength for each analyte was chosen at the absorption maximum between 200 and 300 nm. Spike-recovery experiments revealed mean recoveries of 91 +/- 7.3% for lanosterol, 103 +/- 5.1% for FF-MAS, 104 +/- 5.5% for T-MAS, 103 +/- 4.5% for free cholesterol and 85 +/- 5.1% for progesterone. The lower recovery value for progesterone was due to a sub-optimal extraction procedure for this particular analyte, as indicated by re-extraction. The minimum amounts of FF-MAS required for quantification were 4 ng/mL and 23 ng/mL for T-MAS and lanosterol. FF-MAS was assayed to approximately 1.6 microM. T-MAS and lanosterol was assayed to about half of this value. No esterification of either MAS or lanosterol could be detected in huFF. Less than 10% of cholesterol was underivatized cholesterol, as more than 10 times the amount of free cholesterol could be assayed after extended saponification. This method can be used for evaluating the accumulation of MAS in huFF and its correlation to oocyte quality and fertilization parameters in in vitro fertilization programmes.

L31 ANSWER 16 OF 19 MEDLINE DUPLICATE 7
1999428610 Document Number: 99428610. PubMed ID: 10497322. Meiosis
activating sterols (**MAS**) and fertility in mammals and man.
Bykov A G; Andersen C Y; Leonardsen L; Baltzen M. (Laboratory of
Reproductive Biology, Juliane Marie Center for Children, Women and
Reproduction, University Hospital of Copenhagen, DK-2100 Copenhagen,
Denmark.. agb.lrb@notes.rh.dk) . JOURNAL OF EXPERIMENTAL-ZOOLOGY, (1999
Oct 15) 285 (3) 237-42. Ref: 34. Journal code: 0375365. ISSN: 0022-104X.
Pub. country: United States. Language: English.

AB In mammals two meiosis activating sterols (**MAS**) have been found
to activate meiotic resumption in mouse oocytes, in vitro. FF-**MAS**
(4, 4-dimethyl-5alpha-cholesta-8,14,24-triene
-3beta-ol) was extracted from human preovulatory follicular
fluid and T-**MAS** (4, 4-dimethyl-5alpha-cholest-8,24-
diene-3beta-ol) from bull testicular tissue. Quite
unexpected, these two sterols, which introduce the cholesterol
biosynthetic pathway from lanosterol, may be locally acting substances
with important physiological function for reproduction. FF-**MAS**
and T-**MAS** are present in the preovulatory follicular fluid of
different mammalian species and have the capacity to initiate resumption
of meiosis in mouse oocyte cultured in the presence of hypoxanthine, a
natural meiosis maturation inhibitor. FF-**MAS** is produced by the
cumulus cells of intact oocyte-cumulus complexes upon FSH-stimulation and
provides the oocyte with a go-signal for the resumption of meiosis. T-
MAS constitutes the vast majority of **MAS** found in the
mammalian testis and in the human ejaculate; in particular a high
concentration is found in the spermatozoa. T-**MAS** may be produced
by the spermatids and the presence of T-**MAS** in spermatozoa may
suggest that T-**MAS** plays a role in fertilization by affecting
the second meiotic division. J. Exp. Zool. (Mol. Dev. Evol.) 285:237-242,
1999.

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L31 ANSWER 17 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1999:404085 Document No.: PREV199900404085. Meiosis-activating sterol (**MAS**)-induced resumption of meiosis uses a different signal
transduction pathway compared to spontaneous-induced oocyte maturation in
mice. Wiersma, A. (1). (1) Dept Pharmacology, NV Organon, Oss Netherlands.
Biology of Reproduction, (1999) Vol. 60, No. SUPPL. 1, pp. 179. Meeting
Info.: Thirty-Second Annual Meeting of the Society for the Study of
Reproduction Pullman, Washington, USA July 31-August 3, 1999 Society for
the Study of Reproduction. ISSN: 0006-3363. Language: English.

L31 ANSWER 18 OF 19 MEDLINE DUPLICATE 8
1998211257 Document Number: 98211257. PubMed ID: 9550087. Synthesis of
meiosis-activating sterols containing fluorine. Wenckens M; Gronvald F;
Hansen J B. (Department of Life Sciences and Chemistry, Roskilde
University, Denmark.) ACTA CHEMICA SCANDINAVICA, (1998 Apr) 52 (4) 503-7.
Journal code: 9012772. ISSN: 0904-213X. Pub. country: Denmark. Language:
English.

AB It is documented that specific types of sterol play a major role in the
resumption of meiosis in oocytes from mice in vitro. 4,4-Dimethyl-5
alpha-cholesta-8,14,24-trien-3 beta-ol (FF-**MAS**) isolated from
human follicular fluid and 4,4-dimethyl-5 alpha-cholesta-8,24-
dien-3 beta-ol (T-**MAS**) isolated from bull
testicular tissue, have been shown to activate (promote) meiosis in vitro.
In order to evaluate the biological activity and stability of such
compounds, new demethylsterol derivatives have been synthesised. Using
diethylaminosulfur trifluoride (DAST) it was possible to synthesise
selected delta 8, delta 14 sterols with mono and difluoro substitution at

C3.

L31 ANSWER 19 OF 19 MEDLINE
1998328572 Document Number: 98328572. PubMed ID: 9665635. Effects of ketoconazole on ovulatory changes in the rat: implications on the role of a meiosis-activating sterol. Tsafriri A; Popliker M; Nahum R; Beyth Y. (Department of Biological Regulation, The Weizmann Institute of Science, Rehovot, Israel.) MOLECULAR HUMAN REPRODUCTION, (1998 May) 4 (5) 483-9. Journal code: 9513710. ISSN: 1360-9947. Pub. country: ENGLAND: United Kingdom. Language: English.

AB In-vitro studies on mouse oocytes have shown that human follicular fluid and bull testes contain an activity which partially overrides the inhibitory action of hypoxanthine on meiosis. This activity was ascribed to two closely related sterols, subsequently named meiosis-activating sterols (**MAS**). We have used a potent inhibitor of sterol synthesis, ketoconazole, in order to test in vivo and in vitro whether **MAS** play a necessary physiological role in the resumption of meiosis in the rat. When administered systemically, ketoconazole (8.3-16.6 mg/rat) suppressed ovulation by 40%. Local unilateral administration of the drug into the ovarian bursa (1.25 mg/bursa) resulted in 75% inhibition of ovulation in comparison with the contralateral ovary. All the ovulated ova in the oviduct were mature. Histological examination of the ketoconazole-treated ovaries revealed mature oocytes trapped in follicles which failed to ovulate. Furthermore, extraction of oocytes from the large follicles of such ovaries revealed that 79% of them were mature. Addition of ketoconazole (0.0001-0.01 mM) to the culture medium did not affect significantly the spontaneous maturation of rat oocytes. However, ketoconazole at a higher concentration (0.1 mM) caused the degeneration of oocytes. Ketoconazole (0.01 mM) did not affect luteinizing hormone (LH)-stimulated oocyte maturation in explanted preovulatory follicles, even though it inhibited follicular progesterone production to levels below the hormone-free control follicles. At higher levels, ketoconazole caused the degeneration of follicles and the enclosed oocytes. In conclusion, using a potent inhibitor of **MAS** we have failed to confirm the suggested obligatory role of **MAS** in the resumption of meiosis in the rat both in vivo and in vitro.

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COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
44.10	45.36

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
-3.10	-3.10

CA SUBSCRIBER PRICE

STN INTERNATIONAL LOGOFF AT 17:25:12 ON 05 SEP 2002

'IN' IS NOT A VALID FIELD CODE
 L26 343 FILE MEDLINE
 L27 603 FILE HCAPLUS
 L28 474 FILE BIOSIS
 'IN' IS NOT A VALID FIELD CODE
 L29 269 FILE EMBASE
 L30 49 FILE WPIDS

TOTAL FOR ALL FILES
 L31 1738 ANDERSEN, T?/AU,IN

=> s l31 and (mas or meiosis activat? substance)
 L32 0 FILE MEDLINE
 L33 2 FILE HCAPLUS
 L34 0 FILE BIOSIS
 L35 0 FILE EMBASE
 L36 1 FILE WPIDS

TOTAL FOR ALL FILES
 L37 3 L31 AND (MAS OR MEIOSIS ACTIVAT? SUBSTANCE)

=> dup rem l37
 PROCESSING COMPLETED FOR L37
 L38 2 DUP REM L37 (1 DUPLICATE REMOVED)

=> d cbib abs 1-2

L38 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2002 ACS
 2002:615351 Process and container with low oxygen content and containing a
 stable **MAS (meiosis activation
 substances)** composition for increasing the fertility of oocytes
 and use in IVF or IVM. Mueller, Lars Klingberg; **Andersen, Tina
 Meinertz** (Novo Nordisk A/S, Den.). PCT Int. Appl. WO 2002062287 A1
 20020815, 22 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA,
 BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE,
 ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
 KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ,
 OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
 UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW:
 AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR,
 IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English).

CODEN: PIXXD2. APPLICATION: WO 2002-DK35 20020117. PRIORITY: DK 2001-189 20010206; DK 2001-382 20010308.

AB A solid, stable compn. contg. a **meiosis activating substance** can be prepd. by adding a protein or a phosphoglyceride in the presence of an atm. having a low content of oxygen, for example in vacuo. A closed container having a low content of oxygen and further contg. **MAS** is claimed. More specifically, a closed container having a low content of oxygen and further contg. a solid compn. with high aq. soly. comprising **MAS** and an additive is claimed. Also claimed is a process for prepg. a closed container having a low content of oxygen and further contg. a solid compn. comprising **MAS** and an additive.

L38 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
2001:208095 Document No. 134:242674 Composition for in vitro IVF containing a **meiosis-activating substance**.

Andersen, Tina Meinertz (Novo Nordisk A/s, Den.). PCT Int. Appl. WO 2001019354 A2 20010322, 11 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-DK500 20000911. PRIORITY: DK 1999-1308 19990916.

AB A compn. useful in connection with in vitro fertilization (IVF) based on a solid **meiosis-activating substance** (**MAS**) or a deriv. thereof with low soly. is described. A **MAS** can be dissolved in an aq. medium using an additive, e.g., a protein or a phosphoglyceride, to obtain a soln. contg. at least 0.001 .mu.g/mL and not more than 0.1 g/mL of **MAS**. For example, solns. were prepd. by mixing (a) 100 .mu.L of ethanolic 4,4-dimethyl-5.alpha.-cholesta-8,14,24-triene-3.beta.-ol (FF-**MAS**) contg. 5.22, 2.5, or 0.5 .mu.g/mL FF-**MAS** and (b) 250 .mu.L of 20% aq. human serum albumin (HSA) in the ratio of FF-**MAS** to HSA of 1:10,000, 1:6667, and 1:2000, resp., and tested on oocytes obtained from immature female mice. Percent of germinal vesicle breakdown (GVB) for the formulations prepd. were 78, 82, and 90%, resp.

=> dis his

(FILE 'HOME' ENTERED AT 16:57:27 ON 05 SEP 2002)

FILE 'REGISTRY' ENTERED AT 16:57:37 ON 05 SEP 2002

E "4,4-DIMETHYL-5-.ALPHA.-CHOLESTA-8,14,24-TRIENE-3-.BETA.-OL"/
E "4,4-DIMETHYL-5-CHOLEST-8,14,24-TRIEN-3-OL"/CN
E "4,4-DIMETHYL-5-CHOLEST-8,14,24-TRIEN-3-OL HEMISUCCINATE"/CN
E "5-CHOLEST-8-8,14-DIEN-3-OL"/CN
E "5-CHOLEST-8,14-DIEN-3-OL"/CN
E " (20S)-CHOLEST-5-EN-3,20-DIOL"/CN
E " (20S)-CHOLEST-5-EN-3,20-DIOL"/CN

FILE 'MEDLINE, HCAPLUS, BIOSIS, EMBASE, WPIDS' ENTERED AT 17:00:54 ON 05 SEP 2002

L1 2756 FILE MEDLINE
L2 10744 FILE HCAPLUS
L3 2615 FILE BIOSIS
L4 2204 FILE EMBASE
L5 827 FILE WPIDS

TOTAL FOR ALL FILES

Searched by: Mary Håle 308-4258 CM-1 1E01

L6 19146 S MAS OR DIMETHYL(5A)CHOLESTA?(10A)TRIENE(5A)OL OR DIMETHYL(3W)
 L7 26 FILE MEDLINE
 L8 36 FILE HCAPLUS
 L9 33 FILE BIOSIS
 L10 23 FILE EMBASE
 L11 15 FILE WPIDS

TOTAL FOR ALL FILES

L12 133 S FF MAS
 L13 55 FILE MEDLINE
 L14 60 FILE HCAPLUS
 L15 59 FILE BIOSIS
 L16 37 FILE EMBASE
 L17 14 FILE WPIDS

TOTAL FOR ALL FILES

L18 225 S (L6 OR L12) AND (MEIOSIS OR MATUR? PROMOT? FACTOR OR CELL DIV

FILE 'REGISTRY' ENTERED AT 17:07:55 ON 05 SEP 2002
 E PHOSPERGLYCID/CN

FILE 'MEDLINE, HCAPLUS, BIOSIS, EMBASE, WPIDS' ENTERED AT 17:08:03 ON 05
 SEP 2002

L19 21 FILE MEDLINE
 L20 21 FILE HCAPLUS
 L21 14 FILE BIOSIS
 L22 12 FILE EMBASE
 L23 2 FILE WPIDS

TOTAL FOR ALL FILES

L24 70 S L18 AND (PROTEIN OR PEPTIDE OR AMINO ACID OR PHOSPERGLYCID? O
 L25 35 DUP REM L24 (35 DUPLICATES REMOVED)
 L26 343 FILE MEDLINE
 L27 603 FILE HCAPLUS
 L28 474 FILE BIOSIS
 L29 269 FILE EMBASE
 L30 49 FILE WPIDS

TOTAL FOR ALL FILES

L31 1738 S ANDERSEN, T?/AU, IN
 L32 0 FILE MEDLINE
 L33 2 FILE HCAPLUS
 L34 0 FILE BIOSIS
 L35 0 FILE EMBASE
 L36 1 FILE WPIDS

TOTAL FOR ALL FILES

L37 3 S L31 AND (MAS OR MEIOSIS ACTIVAT? SUBSTANCE)
 L38 2 DUP REM L37 (1 DUPLICATE REMOVED)

=> s (l6 or l12) and activ? substance?

L39 5 FILE MEDLINE
 L40 17 FILE HCAPLUS
 L41 7 FILE BIOSIS
 L42 5 FILE EMBASE
 L43 29 FILE WPIDS

TOTAL FOR ALL FILES

L44 63 (L6 OR L12) AND ACTIV? SUBSTANCE?

=> s l44 and (protein or peptide or amino acid or phosperglycid? or phospherglycid?
 or ?glycid?)

L45 1 FILE MEDLINE
 L46 3 FILE HCAPLUS
 L47 1 FILE BIOSIS
 L48 1 FILE EMBASE
 L49 4 FILE WPIDS

TOTAL FOR ALL FILES

L50 10 L44 AND (PROTEIN OR PEPTIDE OR AMINO ACID OR PHOSPERGLYCID? OR
PHOSPHERGLYCID? OR ?GLYCID?)

=> s l50 not l24

L51 0 FILE MEDLINE
L52 0 FILE HCAPLUS
L53 0 FILE BIOSIS
L54 0 FILE EMBASE
L55 3 FILE WPIDS

TOTAL FOR ALL FILES

L56 3 L50 NOT L24

=> d 1-3

L56 ANSWER 1 OF 3 WPIDS (C) 2002 THOMSON DERWENT
AN 2001-005775 [01] WPIDS
DNC C2001-001140
TI Halva.
DC D13
IN BOLOBAN, L G
PA (BOLO-I) BOLOBAN L G
CYC 1
PI RU 2152729 C1 20000720 (200101)* A23G003-00
ADT RU 2152729 C1 RU 1999-126411 19991222
PRAI RU 1999-126411 19991222
IC ICM A23G003-00

L56 ANSWER 2 OF 3 WPIDS (C) 2002 THOMSON DERWENT
AN 2000-671400 [65] WPIDS
DNC C2000-203446
TI Correcting additive for macaroni dough and method of preparing macaroni
products.
DC D11
IN IVANOVA, N K; KALININA, M A; SHNEIDER, T I
PA (BREA) BREAD BAKING IND RES INST; (MAKA-R) MAKARON-SERVIS STOCK CO
CYC 1
PI RU 2151525 C1 20000627 (200065)* A23L001-16
ADT RU 2151525 C1 RU 1999-103541 19990223
PRAI RU 1999-103541 19990223
IC ICM A23L001-16
ICS A21D002-00

L56 ANSWER 3 OF 3 WPIDS (C) 2002 THOMSON DERWENT
AN 2000-541617 [49] WPIDS
DNC C2000-160976
TI Cosmetic means for skin care harmonia-n or harmonia-r.
DC B04 D16 D21
IN BACHINSKII, A G; KOCHNEVA, G V; SELIVANOV, B A; SERPINSKII, O I;
SIVOLOBOVA, G F; TATKOV, S I; TSIVKOVSKII, R YU
PA (SINA-R) SIBE NATURAL COSMETICS RES PRODN CENTRE
CYC 1
PI RU 2142785 C1 19991220 (200049)* A61K007-48
ADT RU 2142785 C1 RU 1997-105300 19970403
PRAI RU 1997-105300 19970403
IC ICM A61K007-48
ICS A61K035-12

=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

FULL ESTIMATED COST

ENTRY

SESSION

31.41

51.85

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

CA SUBSCRIBER PRICE

ENTRY

SESSION

-1.24

-1.24

STN INTERNATIONAL LOGOFF AT 17:13:45 ON 05 SEP 2002

=> File .Biotech
=> s (Meiosis activat? substance? or MAS)
L1 24471 (MEIOSIS ACTIVAT? SUBSTANCE? OR MAS)

=> s (Dimethyl(5a)cholesta?(10a)treine?(3a)ol)
L2 0 (DIMETHYL(5A) CHOLESTA?(10A) TREINE?(3A) OL)

=> s (hemisuccin? or cholesta?(5a)dien?(3a)ol)
4 FILES SEARCHED...
L3 9861 (HEMISUCCIN? OR CHOLESTA?(5A) DIEN?(3A) OL)

=> s (dimethyl? or cholest?(5a)treine?(3a)ol)
L4 1346859 (DIMETHYL? OR CHOLEST?(5A) TREINE?(3A) OL)

=> s l1 or l3 or l4 and (additive#)
L5 180999 L1 OR L3 OR L4 AND (ADDITIVE#)

=> s l5 and (protein# or serum albumin or human serum albumin or HSA)
L6 29427 L5 AND (PROTEIN# OR SERUM ALBUMIN OR HUMAN SERUM ALBUMIN OR HSA)

=> s l6 and (recombinant)
L7 7722 L6 AND (RECOMBINANT)

=> s l7 and (enzyme#)
L8 6998 L7 AND (ENZYME#)

=> s l8 and (phosphoglyceride or phosphatidylethanolamine or phosphatidylcholine or phosphatidylserine or phosphatidylinositol)
L9 1802 L8 AND (PHOSPHOGLYCERIDE OR PHOSPHATIDYLETHANOLAMINE OR PHOSPHATIDYLCHOLINE OR PHOSPHATIDYLSERINE OR PHOSPHATIDYINOSITOL)

=> s l9 and (water or aqueous)
L10 1796 L9 AND (WATER OR AQUEOUS)

=> s l10 and (composition or solution)
L11 1790 L10 AND (COMPOSITION OR SOLUTION)

=> s l11 and (meiosis or matur? or promot? factor or cell divis?)
L12 1533 L11 AND (MEIOSIS OR MATUR? OR PROMOT? FACTOR OR CELL DIVIS?)

=> s l12 and (protein or peptide or amino acid or phospherglycid? or ?glycid?)
2 FILES SEARCHED...
6 FILES SEARCHED...
L13 1533 L12 AND (PROTEIN OR PEPTIDE OR AMINO ACID OR PHOSPERGLYCID? OR ?GLYCID?)

=> s l13 and (organic solvent)
L14 51 L13 AND (ORGANIC SOLVENT)

=> s l14 and (germinal vehicle breakdown or GVB)
L15 1 L14 AND (GERMINAL VEHICLE BREAKDOWN OR GVB)

=> d l15 bib ab

L15 ANSWER 1 OF 1 USPATFULL on STN
AN 2002:299266 USPATFULL
TI **Composition** for IVF
IN Andersen, Tina Meinertz, Horsholm, DENMARK
Muller, Lars Klingberg, Ballerup, DENMARK
PI US 2002166789 A1 20021114
AI US 2002-68224 A1 20020205 (10)
PRAI DK 2001-189 20010206
DK 2001-382 20010308
US 2001-273162P 20010302 (60)
DT Utility

FS APPLICATION
LREP Reza Green, Esq., Novo Nordisk of North America, Inc., Suite 6400, 405
Lexington Avenue, New York, NY, 10174-6401
CLMN Number of Claims: 42
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 643

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A solid, stable **composition** containing a **meiosis
activating substance** can be prepared by adding a
protein or a **phosphoglycid** in the presence of an
atmosphere having a low content of oxygen, for example in vacuo.

=> s Andersen, Tina Meinertz?/au
L16 8 ANDERSEN, TINA MEINERTZ?/AU

=> s l14 and l16
L17 1 L14 AND L16

=> d l17 bib ab

L17 ANSWER 1 OF 1 USPATFULL on STN

AN 2002:299266 USPATFULL

TI **Composition** for IVF

IN **Andersen, Tina Meinertz**, Horsholm, DENMARK

Muller, Lars Klingberg, Ballerup, DENMARK

PI US 2002166789 A1 20021114

AI US 2002-68224 A1 20020205 (10)

PRAI DK 2001-189 20010206

DK 2001-382 20010308

US 2001-273162P 20010302 (60)

DT Utility

FS APPLICATION

LREP Reza Green, Esq., Novo Nordisk of North America, Inc., Suite 6400, 405
Lexington Avenue, New York, NY, 10174-6401

CLMN Number of Claims: 42

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 643

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A solid, stable **composition** containing a **meiosis
activating substance** can be prepared by adding a
protein or a **phosphoglycid** in the presence of an
atmosphere having a low content of oxygen, for example in vacuo.

=> dup rem l14

PROCESSING COMPLETED FOR L14

L18 51 DUP REM L14 (0 DUPLICATES REMOVED)

=> s l14 and (human serum albumin or HSA)

L19 9 L14 AND (HUMAN SERUM ALBUMIN OR HSA)

=> d l19 1-9 bib ab

L19 ANSWER 1 OF 9 USPATFULL on STN

AN 2003:225302 USPATFULL

TI **Compositions and methods for treatment of neoplastic disease**

IN **Terman, David S.**, Pebble Beach, CA, UNITED STATES

PI US 2003157113 A1 20030821

AI US 2000-751708 A1 20001228 (9)

PRAI US 1999-173371P 19991228 (60)

DT Utility

FS APPLICATION

LREP David S. Terman, P.O. Box 987, Pebble beach, CA, 93953
CLMN Number of Claims: 60
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 15804

AB The present invention comprises compositions and methods for treating a tumor or neoplastic disease in a host, The methods employ conjugates comprising superantigen polypeptides, nucleic acids with other structures that preferentially bind to tumor cells and are capable of inducing apoptosis. Also provided are superantigen-glycolipid conjugates and vesicles that are loaded onto antigen presenting cells to activate both T cells and NKT cells. Cell-based vaccines comprise tumor cells engineered to express a superantigen along with glycolipids products which, when expressed, render the cells capable of eliciting an effective anti-tumor immune response in a mammal into which these cells are introduced. Included among these compositions are tumor cells, hybrid cells of tumor cells and accessory cells, preferably dendritic cells. Also provided are tumoricidal T cells and NKT cells devoid of inhibitory receptors or inhibitory signaling motifs which are hyperresponsive to the the above compositions and lipid-based tumor associated antigens that can be administered for adoptive immunotherapy of cancer and infectious diseases.

L19 ANSWER 2 OF 9 USPATFULL on STN

AN 2002:329426 USPATFULL

TI Polymer combinations that result in stabilized aerosols for gene delivery to the lungs

IN Zou, Yiyu, Bronx, NY, UNITED STATES

Perez-Soler, Roman, New York, NY, UNITED STATES

PI US 2002187105 A1 20021212

AI US 2002-61444 A1 20020201 (10)

PRAI US 2001-266174P 20010201 (60)

DT Utility

FS APPLICATION

LREP FULBRIGHT & JAWORSKI L.L.P., A REGISTERED LIMITED LIABILITY PARTNERSHIP, SUITE 2400, 600 CONGRESS AVENUE, AUSTIN, TX, 78701

CLMN Number of Claims: 126

ECL Exemplary Claim: 1

DRWN 8 Drawing Page(s)

LN.CNT 5666

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The use of non-viral delivery of therapeutically effective compositions through aerosol for therapy or research purpose has been limited by the low efficiency mainly caused by an inefficient delivery system and destruction of formulation (gene and/or delivery system) by aerosol shearing power. This invention develops formulations that are established polymer combination formulations. The formulations are highly efficient in delivering genes in vivo through aerosol and are able to protect the delivered gene from the destruction by aerosol shearing power.

L19 ANSWER 3 OF 9 USPATFULL on STN

AN 2002:315069 USPATFULL

TI Compositions and methods for treatment of neoplastic disease

IN Terman, David S., Pebble Beach, CA, UNITED STATES

PI US 2002177551 A1 20021128

AI US 2001-870759 A1 20010530 (9)

PRAI US 2000-208128P 20000531 (60)

DT Utility

FS APPLICATION

LREP David S. Terman, P.O. Box 987, Pebble Beach, CA, 93953

CLMN Number of Claims: 30

ECL Exemplary Claim: 1

DRWN 3 Drawing Page(s)

LN.CNT 17323

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention comprises compositions and methods for treating a tumor or neoplastic disease in a host, The methods employ conjugates comprising superantigen polypeptides, nucleic acids with other structures that preferentially bind to tumor cells and are capable of inducing apoptosis. Also provided are superantigen-glycolipid conjugates and vesicles that are loaded onto antigen presenting cells to activate both T cells and NKT cells. Cell-based vaccines comprise tumor cells engineered to express a superantigen along with glycolipids products which, when expressed, render the cells capable of eliciting an effective anti-tumor immune response in a mammal into which these cells are introduced. Included among these compositions are tumor cells, hybrid cells of tumor cells and accessory cells, preferably dendritic cells. Also provided are tumoricidal T cells and NKT cells devoid of inhibitory receptors or inhibitory signaling motifs which are hyperresponsive to the the above compositions and lipid-based tumor associated antigens that can be administered for adoptive immunotherapy of cancer and infectious diseases.

L19 ANSWER 4 OF 9 USPATFULL on STN

AN 2002:299266 USPATFULL

TI **Composition** for IVF

IN Andersen, Tina Meinertz, Horsholm, DENMARK

Muller, Lars Klingberg, Ballerup, DENMARK

PI US 2002166789 A1 20021114

AI US 2002-68224 A1 20020205 (10)

PRAI DK 2001-189 20010206

DK 2001-382 20010308

US 2001-273162P 20010302 (60)

DT Utility

FS APPLICATION

LREP Reza Green, Esq., Novo Nordisk of North America, Inc., Suite 6400, 405

Lexington Avenue, New York, NY, 10174-6401

CLMN Number of Claims: 42

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 643

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A solid, stable **composition** containing a **meiosis activating substance** can be prepared by adding a **protein** or a **phosphoglycid** in the presence of an atmosphere having a low content of oxygen, for example in vacuo.

L19 ANSWER 5 OF 9 USPATFULL on STN

AN 2002:272939 USPATFULL

TI PEI: DNA vector formulations for in vitro and in vivo gene delivery

IN Cristiano, Richard J., Pearland, TX, UNITED STATES

Yamashita, Motoyuki, Kochi City, JAPAN

PA Board of Regents, The University of Texas System (U.S. corporation)

PI US 2002151060 A1 20021017

AI US 2001-962922 A1 20010925 (9)

PRAI US 2000-235237P 20000925 (60)

US 2000-235635P 20000926 (60)

DT Utility

FS APPLICATION

LREP FULBRIGHT & JAWORSKI L.L.P., A REGISTERED LIMITED LIABILITY PARTNERSHIP,

SUITE 2400, 600 CONGRESS AVENUE, AUSTIN, TX, 78701

CLMN Number of Claims: 141

ECL Exemplary Claim: 1

DRWN 31 Drawing Page(s)

LN.CNT 7002

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates generally to the fields of nucleic acid transfection. More particularly, it concerns novel polycation:nucleic acid compositions, methods of preparation of such compositions and

methods of transfecting cells with such compositions.

L19 ANSWER 6 OF 9 USPATFULL on STN
AN 2002:224605 USPATFULL
TI Lipid soluble steroid prodrugs
IN Unger, Evan C., Tucson, AZ, United States
Shen, DeKang, Tucson, AZ, United States
PA Imarx Therapeutics, Inc., Tucson, AZ, United States (U.S. corporation)
PI US 6444660 B1 20020903
AI US 2000-496761 20000203 (9)
RLI Division of Ser. No. US 1997-851780, filed on 6 May 1997, now patented,
Pat. No. US 6090800
DT Utility
FS GRANTED
EXNAM Primary Examiner: Badio, Barbara P.
LREP Woodcock Washburn LLP
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 6452
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is directed to novel lipid soluble steroid
prodrugs, compositions comprising steroid prodrugs, and uses of the
same.

L19 ANSWER 7 OF 9 USPATFULL on STN
AN 2001:55447 USPATFULL
TI Pretargeting methods and compounds
IN Meyer, Damon L., Bellevue, WA, United States
Mallett, Robert W., Seattle, WA, United States
PA NeoRx Corporation, Seattle, WA, United States (U.S. corporation)
PI US 6217869 B1 20010417
AI US 1997-926336 19970905 (8)
RLI Continuation of Ser. No. US 1994-351005, filed on 7 Dec 1994, now
abandoned Continuation-in-part of Ser. No. US 163188, now abandoned
Continuation-in-part of Ser. No. US 1992-995381, filed on 23 Dec 1992,
now abandoned Continuation-in-part of Ser. No. US 1992-895588, filed on
9 Jun 1992, now patented, Pat. No. US 5283342
DT Utility
FS Granted
EXNAM Primary Examiner: Saunders, David
LREP Seed Intellectual Property Law Group PLLC
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 12 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 6397
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods, compounds, compositions and kits that relate to pretargeted
delivery of diagnostic and therapeutic agents are disclosed.

L19 ANSWER 8 OF 9 USPATFULL on STN
AN 2000:91955 USPATFULL
TI Lipid soluble steroid prodrugs
IN Unger, Evan C., Tucson, AZ, United States
Shen, DeKang, Tucson, AZ, United States
PA Imarx Pharmaceutical Corp., Tucson, AZ, United States (U.S. corporation)
PI US 6090800 20000718
AI US 1997-851780 19970506 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Dees, Jose' G.; Assistant Examiner: Badio, Barbara
LREP Woodcock Washburn Kurtz Mackiewicz & Norris LLP
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN No Drawings

LN.CNT 6285

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to novel lipid soluble steroid
prodrugs compositions comprising steroid prodrugs, and uses of the same.

L19 ANSWER 9 OF 9 USPATFULL on STN

AN 2000:7398 USPATFULL

TI Biotinamido-n-methylglycyl-seryl-o-succinamido-benzyl dota

IN Theodore, Louis J., Lynnwood, WA, United States

Kasina, Sudhakar, Kirkland, WA, United States

Reno, John M., Brier, WA, United States

Gustavson, Linda M., Seattle, WA, United States

PA NeoRx Corporation, Seattle, WA, United States (U.S. corporation)

PI US 6015897 20000118

AI US 1996-645211 19960513 (8)

RLI Division of Ser. No. US 1994-351005, filed on 7 Dec 1994, now abandoned
which is a continuation-in-part of Ser. No. US 1993-163188, filed on 7
Dec 1993, now abandoned which is a continuation-in-part of Ser. No. WO
1993-US5406, filed on 7 Jun 1993 which is a continuation-in-part of Ser.
No. US 1992-995381, filed on 23 Dec 1992, now abandoned which is a
continuation-in-part of Ser. No. US 1992-895588, filed on 9 Jun 1992,
now patented, Pat. No. US 5283342

DT Utility

FS Granted

EXNAM Primary Examiner: Chan, Christina Y.; Assistant Examiner: Gambel,
Phillip

LREP Seed and Berry LLP

CLMN Number of Claims: 1

ECL Exemplary Claim: 1

DRWN 12 Drawing Figure(s); 7 Drawing Page(s)

LN.CNT 6303

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods, compounds, compositions and kits that relate to pretargeted
delivery of diagnostic and therapeutic agents are disclosed.
Biotinamido-N-methylglycyl-seryl-O-succinamido-benzyl DOTA is disclosed.

---Logging off of STN---

ENTER DISPLAY FORMAT (STD):END

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Executing the logoff script...

=> LOG Y

STN INTERNATIONAL LOGOFF AT 13:20:55 ON 29 AUG 2003